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Comparison of first admission hemogram parameters and chest computed tomography findings of pediatric COVID-19 patients

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Abstract

Aim : We use computed tomography, which is one of the frequently used imaging tests, both as a disease diagnosis method and to follow the clinical course in COVID-19 patients. This also means radiation exposure. Radiation exposure, especially in pediatric patients, can cause life-threatening diseases. Is there a blood parameter that will reduce this undesirable event and allow estimation of computed tomography findings? Are hemogram analysis, one of the most commonly used blood tests, and tomography findings of the disease related? We designed this study based on the questions.

Material and Methods: Among the patients under the age of 18 who applied to the emergency department, those with a positive reverse transcription-polymerase chain reaction (RT-PCR) and chest CT and hemogram were included in the study. Chest CT findings were classified according to the CO-RADS classification. We compared the CO-RADS classification with hemogram parameters and the ratios of these parameters.

Results: Platelet-to-lymphocyte ratio (PLR) rates were found to be significantly lower as imaging findings became more severe (<0.05). The ratio of MedianPlatelet Volume and Platelet (MPV/Plt) was found to be significantly higher as the imaging findings worsened ($p<0.05$). When the relationship between laboratory parameters according to imaging groups in our study was evaluated, there was a moderate negative correlation between lymphocyte and platelet levels and imaging findings ($p<0.05$). A moderate positive correlation with the monocyte level was found ($p<0.05$).

Discussion: For the CO-RADS classification, it can be said that the patient was established to classify possible COVİD-19 patients only according to chest CT. There is no study in the literature on the classification of pediatric patients with RT-PCR positive definite COVID-19 according to chest CT scans and the comparison of laboratory findings of patients with this classification. The combination of laboratory parameters and CO-RADS classification will guide clinicians in pediatric COVID-19 patient management.

Keywords

Pediatric COVID-19, CO-RADS, Emergency Department, Hemogram Parameters

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Introduction

The disease identified as COVID-19, meaning "coronavirus disease 2019", by the World Health Organization (WHO) in February 2020 was first detected in Wuhan Province of Hubei state in China. Since then, the rapidly spreading disease has spread country-wide in China and all over the globe, and a pandemic was announced by the WHO on March 11, 2020. Coronaviruses are human and animal pathogens that can cause disease and cause the clinical presentation of acute severe respiratory syndrome coronavirus 2 (SARS-CoV-2) (available at: http://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 and https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020). COVID-19 is rare in children compared with adults. According to data from the Centers for Disease Control and Prevention (CDC) in the United States of America, pediatric COVID-19 cases account for approximately 9% of total COVID-19 cases [https://www.cdc.gov/covid-data-tracker/index.html#demographics]. A previous study focusing on minor patients with SARS-CoV-2 confirmed by laboratory analysis emphasized that COVID-19 may be observed in children at any age, with a prevalence according to age distribution: 7% below 1 month of age, 22% between 1 month and 1 year; 10% between 1 year and 2 years; 11% between 2 years and 5 years; 16% between 5 years and 10 years; and 34% between 10 years and 18 years [1]. Spread from COVID-19 patients at home is the most common source of spread in the majority of pediatric cases [2,3]. The literature review stressed that COVID-19 was spread by adults; however, the spread of COVID-19 by asymptomatic children was also considered [4-6]. A review of hospitalization rates due to COVID-19 revealed higher hospitalization rates in children below 2 years of age than in other age groups [5-7].

A comprehensive study that also reviewed laboratory data of children with COVID-19 below 18 years of age concluded that hemogram parameters of many patients were normal. However, there are studies reporting higher lymphopenia levels [8], a study revealing a neutropenia rate of 13% [9], and studies indicating that neutrophilia and lymphopenia were detected when the clinical manifestation became severe [10].

A previous study conducted on 674 pediatric patients with COVID-19 infection using imaging methods performed computed tomography (CT) in 605 patients. Among children who underwent CT, 29% presented frosted glass findings, including bilateral findings in 23% and unilateral findings in 27%; however, approximately 33% of the children who had CT examinations did not present any findings [8].

We aimed to compare thoracic CT findings with hemogram parameters and the ratio of these parameters in patients below 17 years of age diagnosed with a positive reverse transcription-polymerase chain reaction.

Material and Methods

This study was conducted in Ankara, the capital city of Turkey; the record system data of patients were reviewed between March 15, 2021, and June 15, 2021. All patients were selected from pediatric patients who were referred to the COVID-19 emergency department. The study included RT-PCR-positive patients below 18 years of age whose thoracic CT scan and hemogram parameters were available. Patients were divided into 5 age groups: 0 to 2 years, 3 to 5 years, 6 to 10 years, 11 to 15 years, and 16 to 17 years. The CT findings of such patients were categorized according to the CO-RADS classification. Patients are evaluated in 7 categories in this system. CO-RADS 0 represents patients who could not be classified due to deficient or insufficient examination because of severe artifacts, whereas CO-RADS 6 represents RT-PCR-positive patients. This includes the categorization of images without any suspicion of COVID-19 in first- and second-category patients. Normal or non-infectious changes are defined as CO-RADS 1; infectious findings beyond COVID-19 are categorized as CO-RADS 2; images suspected for COVID-19 or any other infection are classified as CO-RADS 3; suspected images of COVID-19 are defined as CO-RADS 4, and typical involvement is classified as CO-RADS 5. The patients who were referred to the pediatric COVID-19 emergency department and had imaging analyses were listed; those with CT scan findings were enrolled (Figure 1).

Statistical analysis

All statistical analyses were performed using SPSS version 20.0 for Windows. The Kolmogorov-Smirnov test and skewness-kurtosis method were used to evaluate the normal distribution of all variables. Descriptive statistical methods were used for demographic analyses of the patients. Chi-square and Fisher's exact tests were used to compare categorical variable rates. Numerical data are expressed as mean ± standard deviation and minimum-maximum values. Nonparametric variables obtained in the study that were carried out within the scope of clinical research were assessed through the Kruskal-Wallis H and Mann-Whitney U statistical tests for statistical evaluation depending on categorical (nominal or ordinal) and numeric independence status. Laboratory parameters were evaluated by the receiver operating characteristic (ROC) curve according to the imaging results of pediatric COVID-19 patients. Parameters including AUC <0.6 and statistically insignificant parameters (P>0.05) were excluded during the evaluation of the ROC analysis. The results were evaluated for significance level at $p<0.05$.

Results

In the present study, 114 pediatric patients who met the research criteria were enrolled between March 15, 2020, and June 15, 2020. The study included 55 males (48.2%) and 59 (51.8%) females. The average age of the pediatric patient group was 10.6±5.9 (median 12) years. The distribution of patients according to age group is shown in Table 1. Imaging findings of patients were divided into groups according to CO-RADS classification. Accordingly, the groups were classified according to tomography imaging as follows: 52.6% (n=60) CO-RADS 1, 9.6% (n=11) CO-RADS 2, 7.9% (n=9) CO-RADS 3, 14% (n=16) CO-RADS 4, and 15.8% (n=18) CO-RADS 5. A statistically significant difference was found between CT imaging findings according to the age groups (x2 2:33.114; p=0.070).

Laboratory parameters of pediatric COVID-19 patients

The imaging findings and laboratory parameters of COVID-19 patients are summarized in Table 2. Lymphocyte and platelet

levels were found to be significantly lower when imaging findings became more severe according to CO-RADS classification (<0.05). The monocyte parameter was significantly higher when imaging findings became more severe (<0.05). The platelet-to-lymphocyte ratio (PLR) was found to be significantly lower when imaging findings became more severe (<0.05). The median platelet volume to platelet (MPV/Plt) ratio was significantly higher when imaging findings became more severe (p<0.05). Evaluation of the association based on imaging groups revealed a moderately negative correlation between lymphocyte and platelet levels of laboratory parameters and imaging findings (<0.05). A moderately positive association was also detected for monocyte levels (<0.05). There were no differences between groups for WBC, neutrophil, MPV, RDW laboratory parameters or neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), or imaging findings (>0.05).

Lymphocyte, Monocyte, PLR, ROC analyses of COVID-19 patients

The AUC, cut-off, sensitivity and specificity of the ROC curve and laboratory parameters were analyzed to guide clinicians in patient monitoring through the imaging findings of COVID-19 patients. The patients were divided into two groups: those without imaging findings (CO-RADS 1-2) and those with imaging findings (CO-RADS 3-5), and cut-off values of laboratory parameters were calculated. Any p-value above 0.05 (p>0.05) was accepted as insignificant. Accordingly, laboratory parameters of WBC, lymphocytes, monocytes, platelets, RDW, and MPV/PLT ratio were accepted as statistically significant

Table 1. Characteristics of COVID-19 patients

Characteristics of COVID-19 patients							P-value
Gender							
Male n (%)	48.2% (n=55)						
Female n (%)	51.8% (n= 59)						
Age (Mean ±SD)	10.6 ±5.9						
Distribution of imaging findings according to age groups							
Age Groups	n(%)	Corads 1 n(%)	Corads 2 n(%)	Corads 3 n(%)	Corads 4 n(%)	Corads 5 n(%)	
0-2n (%)	15 (13.4)	4(6.7)	-	5 (55.6)	2 (13.3)	4 (26.7)	
3-5n (%)	11 (9.8)	5 (8.3)	1 (9.1)	-	5 (31.3)	-	
6-10n (%)	18 (15.2)	9 (15)	2 (18.2)	-	3 (18.8)	3 (17.6)	
11-15n (%)	33 (29.5)	23 (38.3)	4 (36.4)	2 (22.2)	1 (6.3)	4 (11.8)	
16.17.9 n(%)	36 (32.1)	19 (31.7)	4 (36.4)	2 (22.2)	5 (31.3)	7 (18.9)	
Total	114 (100)	60 (52.6)	11 (9.6)	9 (7.9)	16 (14)	18 (15.8)	0.007

Any p-value below 0.05 (p<0.05) was accepted statistically significant.

Table 2. Laboratory parameters according to imaging findings

Laboratory parameters	Corads 1 (Mean±SD)	Corads 2 (Mean±SD)	Corads 3 (Mean±SD)	Corads 4(Mean±SD)	Corads 5 (Mean±SD)	P-value
WBC (4.0-10.0 × 10^9/L)	6.6 ±3.5	7.8 ±3.1	9.03 ±7.16	10.11 ±6.7	10.15 ±6.9	0,065
Neutrophils (2.0-6.0× 10^9/L)	4.4 ±2.5	4.3 ±3.5	3.6 ±1.6	4.43 ±4.3	7.2 ±2.3	0.84
WBC (1.1-3.2 × 10^9/L)	4.3 ±4.4	3.2 ±2.2	2.1 ±2.15	1.9 ±1.6	1.6 ±1.1	0.005*
Monocyte 109/L	0.3 ±0.21	0.37 ±0.24	0.48 ±0.3	0.54 ±0.37	0.84 ±0.56	0.000*
Platelet x 109/L	441 ±144	291 ±117	286.2 ±119	271 ±89	223 ±64	0.025*
Mean platelet volume fl	8.6 ±1.08	8.86 ±1.3	9.2 ±1.4	9.28 ±1.15	9.5 ±1.3	0,283
Red blood cell distribution width-CV %	13.59 ±1.6	13.65 ±1.6	13.7 ±2.7	14.3 ±2.2	15.35 ±1.9	0,05
NLR	1.6 ±1.3	2.53 ±2.2	5.2 ±4.8	8.8 ±5.3	9.3 ±7.1	0.82
PLR	266 ±99	139 ±74	132.3 ±64	101 ±71	82 ±55	0.006*
MLR	1.4 ±0.8	2.1 ±1.3	1.7 ±1.8	2.4 ±2.2	3.7 ±1.9	0,695
MPV/Platelet	3.3 ±1	3.2 ±1	3.4 ±0.6	4.1 ±1.7	7 ±1.3	0.005*

Kruskal-Wallis H test was used for statistical analysis. * A p<0.05 was considered significant. SD: Standard Deviation. NLR: neutrophil-lymphocyte ratio, MLR: monocyte-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

Table 3. Cut-off, sensitivity and specificity results of hemogram parameters

Laboratory parameters	Cut-off value	AUC	P value	95% Confidence Interval (Lower Limit- Upper Limit)	Sensitivity %	Specificity %
WBC	7.98	0.658	0.005	0.553-0.764	53.5	79.7
Lymphocyte	1.67	0.607	0.048	0.634-0.834	65.1	51.7
Monocyte	0.71	0.717	0.000	0.496-0.714	55.8	62.5
Platelet	230.5	0.660	0.004	0.556-0.765	69.8	53.2
RDW	14.4	0.617	0.038	0.511-0.723	67.4	50.3
MPV/Plt	112.1	0.635	0.017	0.525-0.745	61.2	61.7

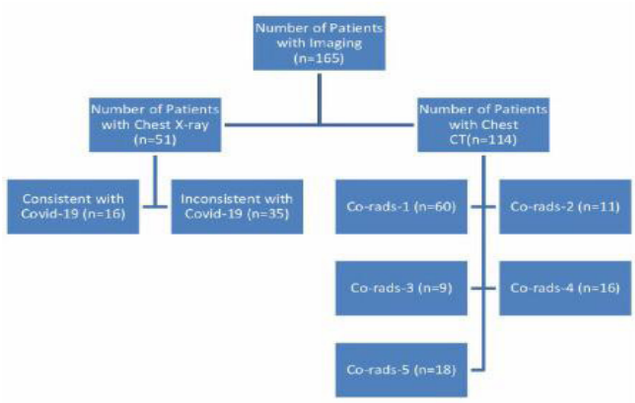

Figure 1. Patient Flow Diagram

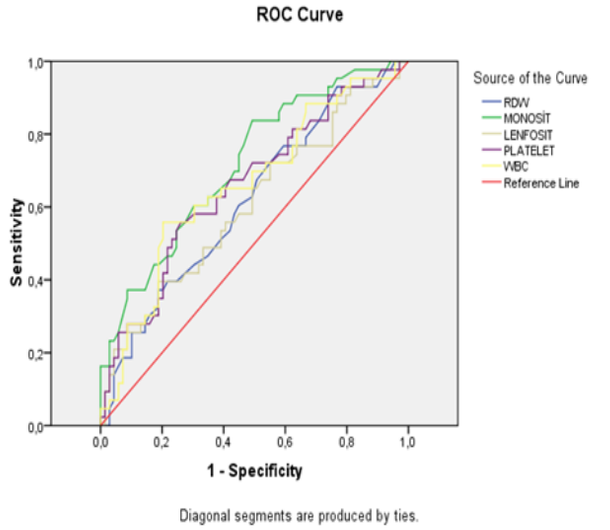

Figure 2. WBC, monocyte and lymphocyte, platelet and RDW ROC curve

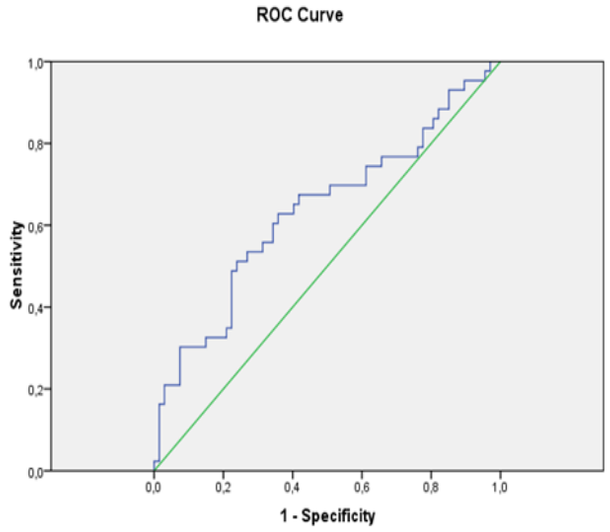

Figure 3. MPV/PLT Ratio

(p<0.05). Table 3 summarizes the ROC curve, AUC, cut-off, sensitivity and specificity for these parameters (Figures 2, 3).

Discussion

This study was conducted to review 114 RT-PCR-positive pediatric patients who underwent chest CT scans. A negative association was detected between severe lesions detected by CT, settlement and progression of typical COVID-19 findings (by CO-RADS classification) and lymphocytes, platelets and PLR; however, a linear association was detected between monocyte count and MPV/PLT.

Studies reviewing the changes in hemogram parameters during COVID-19 infection have been published in the literature. Tezer H. et al. reported in their manuscript on COVID-19 in children that lymphocyte counts may be decreased. However, the association between the severity of COVID-19 infection and imaging was not mentioned [11]. González-Dambrauskas S. et al. indicated in their study on pediatric critical care and COVID-19 that critical patients present lymphopenia and leukocytosis. The aforementioned study did not include 17 pediatric patients monitored in the intensive care unit [12]. Song W. et al. included 16 children in their study with the title of clinical characteristics of pediatric patients, and lymphopenia was detected in 1 patient. Imaging and laboratory findings were not compared in this study, although CT images of the patients were included in the study [13]. Ma H. et al. enrolled 158 patients, including 50 RT-PCR-positive patients, in their study and detected lymphopenia in 30% and thrombocytopenia in 16% of PCR-positive patients. However, the severity of CT findings or disease was not compared with the aforementioned findings [14]. Dink Y. et al. detected lymphopenia-leukocytopenia as a common laboratory finding in their meta-analysis; however, they did not include other hemogram parameters or ratios [15]. Ghayda Abou R. et al. stated in their meta-analysis that lymphopenia is a patognomonic finding, and there is an association between disease severity and lymphopenia level [16]. Comparison of our findings with other studies stated above advances our study due to its larger patient series and positive PCR values in all patients; moreover, our findings are supported by current data in the literature. In our study, where typical/diffuse findings (CO-RADS classification) and laboratory parameters were compared, a positive significant association and PLR ratio between monocyte count, MPV/PLT ratio and disease severity and a negative significant association between PLR ratio and disease severity by imaging were important outcomes that should be emphasized because such evaluations were not sufficiently addressed in pediatric patients in the literature. Monocytes are an important blood component that increases in infectious conditions, including viral and bacterial infections [17]. MPV is higher in conditions presenting with thrombocytopenia, including sepsis, immune thrombocytopenia and respiratory diseases [18]. Such results were not surprising in our findings.

A previous study on leukocyte levels, which were not significantly associated with CT findings, reported that leukocyte levels were normal in 88% of the patients [13]. A review of the meta-analysis reveals that there are studies reporting an increase in the neutrophil count in pediatric COVID-19 infection; however,

other studies indicate a decrease in the neutrophil count. This variability in the neutrophil value detected in pediatric patients with COVID-19 infection explains why the NLR rate, which provides significant results in adults with COVID-19 infection, is also not significant in children [16]. Although monocyte and lymphocyte values were found to be significantly correlated with CT image classification, the MLR ratio was not significant in our study. Further multicenter studies with a prospective design considering the clinical conditions in larger patient series should focus on these parameters.

Analysis of chest CT results of patients included in our study revealed findings for COVID-19-induced pneumonia in 38% of the patients. The ratio of PCR-positive patients without CT findings was approximately 50%; this finding complies with the data obtained from a meta-analysis conducted by Merkus JFM P. et al. [19].

CO-RADS is a system developed to evaluate the suspicion of COVID-19 infection in chest CT and to standardize communication. A previous study on the evaluation of CO-RADS reported that 93% of patients categorized as CO-RADS 5 were RT-PCR-positive. In the aforementioned study, 7% of patients classified as CO-RADS 3 were not clinically considered to have COVID-19 and were RT-PCR-negative [20]. A comprehensive study reviewed RT-PCR-positive pediatric patients with CT findings consistent with COVID-19 and concluded that half of the patients were below 2.5 years of age [14]. The CO-RADS classification was reviewed according to the age groups in our study; the age group of 0 to 2 years had the highest level of CT findings consistent with CT findings by 73%.

Conclusion

The CO-RADS classification was only established to classify possible COVID-19 patients based on thoracic CT. There is no study on the classification of pediatric patients diagnosed with COVID-19 by positive RT-PCR evidence according to thoracic CT scans or a comparison of laboratory findings of the patients in the literature. The combination of laboratory parameters and CO-RADS classification could guide clinicians in pediatric COVID-19 patient management. Further randomized and controlled trials with larger patient series are required to consolidate current findings and to address parameters without any significant associations.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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